**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION**
**DECISION SUMMARY**
**DEVICE ONLY TEMPLATE**

**A. 510(k) Number:**
k040885

**B. Purpose for Submission:**
New device

**C. Analyte:**
Anti-gp210 antibodies (nuclear pore membrane protein)

**D. Type of Test:**
semi-quantitative enzyme-linked immunosorbent assay (ELISA)

**E. Applicant:**
INOVA Diagnostics

**F. Proprietary and Established Names:**
QUANTA Lite™ gp210 ELISA

**G. Regulatory Information:**

1. Regulation section:
   21 CFR §866.5090, Antimitochondrial Antibody Immunological Test System
2. Classification:
   Class II
3. Product Code:
   NRI, Autoantibodies, Nuclear Pore Glycoprotein (gp210)
4. Panel:
   Immunology 82

**H. Intended Use:**

1. Intended use(s):
   The QUANTA Lite™ gp210 kit is an enzyme-linked immunosorbent assay (ELISA) for the semi-quantitative detection of anti-gp210 antibody of the IgG class in human serum. The test is intended to aid in the diagnosis of primary biliary cirrhosis (PBC).
2. Indication(s) for use:
   The QUANTA Lite™ gp210 kit is an enzyme-linked immunosorbent assay (ELISA) for the semi-quantitative detection of anti-gp210 antibody of the IgG class in human serum. The test is intended to aid in the diagnosis of primary biliary cirrhosis (PBC).
3. Special condition for use statement(s):
   For prescription use only.
4. Special instrument Requirements:
   Microwell plate reader capable of measuring OD at 450nm and 620 nm for dual wavelength readings.

**I. Device Description:**
The QUANTA Lite gp210 ELISA consists of a polystyrene microwell ELISA plate coated with purified gp210 peptide antigen, ELISA negative, low positive and high

positive controls, sample diluent, wash concentrate, goat anti-human IgG horseradish peroxidase conjugate, TMB chromogen, and stop solution.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):
   QUANTA Lite™ M2 ELISA
2. Predicate K number(s):
   k933180
3. Comparison with predicate:

| Similarities | | |
|---|---|---|
| **Item** | **Device** | **Predicate** |
| | **Gp210 ELISA** | **M2 ELISA** |
| Intended Use | An aid in the diagnosis of primary biliary cirrhosis | Same |
| Method | ELISA | Same |
| Solid phase | Coated polystyrene microwell plates | Same |
| Sample diluent | Tris-buffered saline, Tween 20, absorbents and protein stabilizers | Same |
| Wash concentrate | Tris-buffered saline and Tween 20 | Same |
| HRP IgG conjugate | Goat anti-human IgG | Same |
| Controls | Negative, low positive and high positive | Same |
| **Differences** | | |
| **Item** | **Device** | **Predicate** |
| | **Gp210 ELISA** | **M2 ELISA** |
| Analyte detected | Anti-gp210 antibodies | Anti-mitochondrial (M2) antibodies |
| Capture antigen | Purified peptide corresponding to a portion of the gp210 protein | Purified mitochondrial M2 antigen (pyruvate dehydrogenase) |

**K. Standard/Guidance Document Referenced (if applicable):**

None referenced

**L. Test Principle:**

The assay utilizes plastic microwells as a solid phase for attachment of a purified peptide corresponding to a portion of the gp210 protein, to coat the plate microwells. Pre-diluted controls and diluted patient sera are added to separate wells, allowing any gp210 antibodies present to bind to the immobilized antigen. Unbound sample is washed away and an enzyme labeled anti-human IgG antibody is added to each well. A second incubation allows the enzyme labeled anti-human IgG to bind to any patient antibodies which have become attached to the microwells. After washing away any unbound enzyme labeled anti-human IgG, the remaining enzyme activity is measured by adding a chromogenic substrate and measuring the intensity of the color that

develops. The assay can be evaluated by spectrophotometrically measuring and comparing the color intensity that develops in the patient wells with the color in the control wells. Results determined with the assay are interpreted as negative, equivocal, or positive and are reported in arbitrary units.

**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:

***a. Precision/Reproducibility:***

Intra-assay performance for the gp210 ELISA was evaluated by testing 10 specimens a total of 6 times each. The samples tested ranged from 5.3 to 140.8 Units with %CV ranging from 0.8 to 11.8%.

| | A | B | C | D | E | F | G | H | I | J |
|---|---|---|---|---|---|---|---|---|---|---|
| Mean units | 83.5 | 113.8 | 140.8 | 5.3 | 5.4 | 18.6 | 29.3 | 21 | 25 | 25.8 |
| SD | 2.0 | 0.9 | 3.5 | 0.6 | 0.6 | 0.9 | 0.7 | 1.2 | 0.9 | 1.2 |
| CV% | 2.4 | 0.8 | 2.5 | 11.2 | 11.8 | 4.8 | 2.5 | 5.5 | 3.0 | 4.8 |

Inter-assay variation was assessed by testing, in duplicate, a panel of 5 specimens twice daily (once in the morning and once in the afternoon) for 3 days. Percent CV ranged from 2.5 to 14.4 Units.

| | HPC | Spec. 1 | Spec. 2 | Spec. 3 | Spec. 4 | Spec. 5 |
|---|---|---|---|---|---|---|
| Mean units | 82.9 | 84.8 | 117.6 | 147.0 | 5.8 | 6.1 |
| SD | 2.1 | 2.99 | 3.86 | 6.06 | 0.70 | 0.88 |
| CV% | 2.5 | 3.5 | 3.3 | 4.1 | 12.1 | 14.4 |

***b. Linearity/assay reportable range:***

No claims were made regarding linearity for the assay. It is a semi-quantitive assay with results reported out as negative (0.0 – 20.0 Units), positive as ≥ 25 Units, or equivocal (20.1 – 24.9 Units) when results are interpreted by comparison to the low positive control value of 25 Units. Specimens giving OD readings above the readable range of the plate reader may be reported as greater than the highest measurable OD, divided by the low positive OD times 25 Units. Alternatively, the sample may be diluted, re-run and a calculated value obtained.

***c. Traceability(controls, calibrators, or method):***

There is no recognized standard or reference material for anti-gp210 antibodies.

***d. Detection limit:***

The determination of detection limit was not relevant for this assay.

***e. Analytical specificity:***

Microbial contaminated, heat-treated, samples with visible particulate, grossly hemolyzed or lipemic specimens should be avoided.

***f. Assay cut-off:***

A panel of 236 asymptomatic, healthy individuals was tested. The panel included subjects from the US (n=187), UK (n=29) and Japan (n=20). Age and gender data were available for 188 specimens and unavailable for 20 specimens. The remaining 28 specimens had only gender data. The ages ranged from 17 to 73 years and included 78 females and 55 males. The average and the median value of anti-gp210 antibody value for the normal population were 3.7 units and 3.4 units respectively. With the exception of one specimen which was 16.5 units, the 235 specimens all had values less than 9.2 uits. Since a negative result was defined as < 20 units, all specimens tested were negative.

2. Comparison studies:

***a. Method comparison with predicate device:***

The sponsor submitted comparison data for 232 samples from 172 PBC patients, and 60 non-PBC (disease controls and normal) subjects. Both assays were negative for all non-PBC samples. Results are summarized below.

| | | QUANTA Lite **M2** ELISA | | |
|---|---|---|---|---|
| | | + | - | Total |
| Quanta Lite **gp210** ELISA | + | 33 | 83 | 116 |
| | - | 12 | 103 | 116 |
| | Total | 45 | 186 | 232 |

Positive agreement = 73.3% (33/45) (95% CI 60.4% to 86.2%)
Negative agreement = 53.4% (103/186) (95% CI 46.2% to 60.6%)
Overall agreement = 58.6% (136/232) (95% CI 52.3% to 64.9%)

The overall agreement between the assays was low because the assays measure different analytes and have different clinical sensitivities and specificities in the PBC population. The clinical sensitivity of the new device (26.1%) was supported by the published literature. The literature also supports the fact that an anti-gp210 antibody assay may detect a subpopulation of PBC patients that are negative for AMA by IFA and/or negative for M2 antibodies measured by ELISA. In the data sets studied, adding the anti-gp210 assay to AMA alone (sensitivity = 79.7%), and to AMA plus M2 ELISA (combined sensitivity = 86%), increased the sensitivity to 90.1% when all three assays are combined.

***b. Matrix comparison:***

Both assay use serum as matrix.

3. Clinical studies:

***a. Clinical sensitivity:***

Clinical sensitivity was established by testing sera from 348 PBC or PBC/AIH (autoimmune hepatitis) subjects. The overall clinical

sensitivity of the assay was 26.1% (91/348 with 2 equivocal results considered as negative).

| Clinical Status | N | Gp210 ELISA positive | Gp210 ELISA equivocal | Gp210 ELISA negative |
|---|---|---|---|---|
| PBC | 343 | 89 | 2 | 252 |
| PBC/AIH | 5 | 2 | 0 | 3 |

***b. Clinical specificity:***

A total of 419 sera from patients with non-PBC liver disease, autoimmune, other conditions (n=183) and normal subjects (n=236) were tested to assess potential cross-reactivity of other disease sera with the assay. All samples were negative.

| Non-PBC or PBC/AIH | N | Gp210 positive | Gp210 negative |
|---|---|---|---|
| HBV | 35 | 0 | 35 |
| HCV | 42 | 0 | 42 |
| SLE | 28 | 0 | 28 |
| AIH 1 | 9 | 0 | 9 |
| AIH 2 | 7 | 0 | 7 |
| RA | 56 | 0 | 56 |
| PSC | 1 | 0 | 1 |
| Scleroderma | 5 | 0 | 5 |
| Normal | 236 | 0 | 0 |
| **Total** | **419** | **0** | **419** (100%) |

***c. Other clinical supportive data (when a and b are not applicable):***

Not applicable.

4. Clinical cut-off:
   See assay cut-off and expected values.
5. Expected values/Reference range:

The prevalence of PBC ranges from estimates of 2 per 100,000 in Japan and Australia to 40 per 100,000 in the US. Studies using IFA, western blot and various ELISA methods suggest anti-gp210 antibodies are present in around 26% of PBC patients.

**N. Conclusion:**

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.